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| 09/735,099 | 12/11/2000 | Johannes Dapprich | 22650-001 CIP | 5343 |

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| EXAMINER | |
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| FORMAN, BETTY J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 11/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/735,099 | DAPPRICH ET AL. | |
| | Examiner | Art Unit | |
| | BJ Forman | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-12,15-19,21,39,40 and 42-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12,15-19,39,40 and 42-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**FINAL ACTION**

***Status of the Claims***

1. This action is in response to papers filed 19 August 2004 in which claims 1, 19, 21, 39, 43, 47 and 50 were amended and claims 13, 14 and 41were canceled. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 19 April 2004 are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant grounds for rejection. New grounds for rejection, necessitated by amendment, are discussed.

Claims 1, 3-12, 15-19, 21, 39-40, 42-55 are under prosecution.

***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claim 19 is rejected under 35 U.S.C. 102(e) as being anticipated by Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claim 19, Engelhardt et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (e.g. mutation Column 12, lines 25-61), contacting the population of nucleic acid molecules with a first targeting element attached to a separation group (i.e. mutation-specific probe with a restriction enzyme site) which specifically binds to the polynucleotide molecule, selectively removing the separation group via digestion dependent upon presence or absence of the mutation and immobilizing the separation groups remaining attached to the separation group complex (Column 12, lines 25-61).

**Response to Arguments**

4. The claims have been amended define the separation group as comprising an immobilizable nucleotide. However, the newly claimed immobilizable nucleotide merely recites an intended use for the nucleotide but does not define or require any structural elements be added to the nucleotide. Hence, the nucleotide is interpreted broadly to encompass any nucleotide.

5. Claims 50-52 and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by Lundeberg et al (U.S. Patent No. 6,482,592, filed 15 September 1998).

Regarding Claim 50, Lundeberg et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (i.e. module-binding site), contacting the population of nucleic acid

molecules with a first targeting element containing a separation group (module) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element (via additional modules, Column 4, lines 9-11) and immobilizing the polynucleotide-targeting element-separation group complex and isolating the complex (Column 11, lines 7-14).

Regarding Claim 51, Lundeberg et al disclose the method wherein the targeting element is an oligonucleotide (Column 5, lines 1-17).

Regarding Claim 52, Lundeberg et al disclose the method wherein the targeting element binds within 20 nucleotides of the distinguishing element (i.e. adjacent, Column 11, lines 21-43).

Regarding Claim 55, Lundeberg et al disclose the method wherein the targeting element-separation group comprises a biotinylated nucleotide i.e. biotinylated oligo (Column 12, lines 42-51).

6. Claims 50-52 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Bukanov et al (Proc. Natl. Acad. Sci. USA, May 1998, 95: 5516-5520).

Regarding Claim 50, Bukanov et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (i.e. opposite strand), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (biotinylated oligonucleotide probe) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element

via PNA opener and immobilizing the polynucleotide-targeting element-separation group (page 5517-page 5518, left column).

Regarding Claim 51, Bukanov et al disclose the method wherein the targeting element is an oligonucleotide (page 5516, right column).

Regarding Claim 52, Bukanov et al disclose the method wherein the targeting element binds within 20 nucleotides of the distinguishing element (i.e. on the opposite strand (page 5517, Fig. 1 and page 5519, left column, third paragraph),

Regarding Claim 55, Bukanov et al disclose the method wherein the targeting element-separation group comprises a biotinylated nucleotide i.e. biotinylated oligo (page 5516, right column).

**Response to Arguments**

7. Applicant asserts that the claims have been amended to require covalent attachment of the separation group to the targeting element. However, the claims have not been so limited. The rejection is maintained.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 3-12, 15-18, 21, 39-40, 42-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ju et al U.S. Patent No. 5,876,936, issued 2 March 1999) in view of Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claim 1, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g). Ju et al specifically teach the "entire sequencing reaction mixtures" are combined with streptavidin coated beads and the beads are immobilized. Following immobilization, the DNA fragments are removed (Column 7, lines 5-32 and Column 9, lines 36-53). This subsequent step of removing the DNA fragments is encompassed by the open claim language "comprising".

Ju et al teach the method wherein the population comprises DNA molecules but they are silent regarding RNA or specific DNAs (e.g. cDNA or genomic DNA) or specific distinguishing elements (e.g. SNP). However, Engelhardt et al teach a similar method of separating a polynucleotide (Claims 112-116) wherein the DNA encompasses any DNA and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23; Column 3, lines 22-45; and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the

genomic DNA analysis of Ju et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

Regarding Claim 3, Ju et al disclose the method wherein the targeting element binds to the distinguishing element (i.e. adjacent to site of terminator incorporation, Column 5, lines 11-13),

Regarding Claim 4, Ju et al disclose the method wherein the targeting element comprises a nucleic acid sequence (i.e. primer, Column 5, lines 3-11).

Regarding Claim 5, Ju et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. primer, Column 5, lines 3-11).

Regarding Claim 6, Ju et al disclose the method wherein the targeting element comprises an extendable 3' hydroxy terminus (i.e. primer, Column 5, lines 3-11).

Regarding Claim 7, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 8, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 9, Ju et al disclose the method wherein the first separation group is attached to the targeting element by extending the oligonucleotide with a polymerase in the presence of biotinylated nucleotide forming an extended oligonucleotide containing immobilizable nucleotide (Column 6, lines 17-47).

Regarding Claim 10, Ju et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. primer, Column 5, lines 3-11).

Regarding Claim 11, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 12, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 13, Ju et al disclose the method wherein the population of molecules is DNA (Column 6, lines 17-22).

Regarding Claim 17, Ju et al disclose the method wherein the substrate is a particle, bead or magnetic bead (Column 7, lines 19-27).

Regarding Claim 18, Ju et al disclose the method further comprising contacting the population with a second targeting element simultaneously and capturing via a second separation group (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 39, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 40, Ju et al disclose the method wherein the oligonucleotide targeting element comprises an extendable 3' hydroxy terminus (i.e. primer, Column 5, lines 3-11).

Regarding Claim 41, Ju et al disclose the method wherein attachment of the separation group to the oligonucleotide is covalent (Column 6, lines 36-47).

Regarding Claim 42, Ju et al disclose the method wherein the first separation group is attached to the targeting element by extending the oligonucleotide with a polymerase in the

presence of biotinylated nucleotide forming an extended oligonucleotide containing immobilizable nucleotide (Column 6, lines 17-47).

Regarding Claim 43, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively and covalently attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 44, Ju et al disclose the method wherein the sequence of interest is an amplified sequence (Column 6, lines 17-31).

Regarding Claim 45, Ju et al disclose the method wherein the attachment occurs through ligation i.e. primer extension ligates nucleotides to the 3' hydroxyl (Column 6, lines 17-47). It is noted that the claim does not require a method step utilizing a specific ligase enzyme. As such, the ligation of the nucleotide onto the primer's 3' end is encompassed by the claimed ligation.

Regarding Claim 46, Ju et al disclose the method wherein covalent attachment occurs by polymerase extension (Column 6, lines 17-47).

**Response to Comments**

10. The claims have been amended to limit the target nucleic acids to genomic DNA or RNA. As cited in the previous Office Action, Engelhardt et al teaches a method similar to Ju wherein

the targets are as newly claimed and further teaches the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23; Column 3, lines 22-45; and Column 12, lines 26-50). Therefore, use of the method taught by Ju to analyze genomic DNA and/or RNA would have been an obvious choice for one of ordinary skill in the art.

The claims have also been amended to recite "wherein said polynucleotide molecule remains bound to said immobilized target element-separation group following removal". However, Ju et al teach this element is taught by Ju et al wherein capture of the extension products is taught (Column 7, lines 5-27). While Ju et al subsequently separates the polynucleotide from the complex, they clearly "capture" and "remove" as claimed. Furthermore, in the subsequent steps of Ju et al teaches removal of reaction mixture components e.g. target, excess primer and etc (Column 7, lines 28-40) which suggests removal of the target is not required, but is an optional next step.

While the instant claims do not require isolation of the polynucleotide, and amendment incorporating this step would not be free of the prior art. Lundeberg et al (U.S. Patent No. 6,482,592) teaches a very similar method to that of Ju et al wherein the subsequent steps of polynucleotide isolation and analysis are performed (Columns 10-11). The reference is made of record, but is not part of the above rejection because are not so limited.

11. Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bukanov et al (Proc. Natl. Acad. Sci. USA, May 1998, 95: 5516-5520) in view of Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claims 53-54, Bukanov et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid

molecules (i.e. control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (i.e. opposite strand), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (biotinylated oligonucleotide probe) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element via PNA opener and immobilizing the polynucleotide-targeting element-separation group (page 5517-page 5518, left column). Bukanov et al teach the method wherein the polynucleotide of interest is genomic DNA page 5517, left column) and they teach their method has diagnostic applications (Abstract) but they do not teach specific diagnostic application e.g. detection of single nucleotide polymorphism (SNP).

Engelhardt et al teach a similar method of separating genomic DNA of interest and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23 and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the genomic DNA analysis of Bukanov et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

12. Claims 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lundeberg et al (U.S. Patent No. 6,482,592, filed 15 September 1998).

Regarding Claims 53-54, Lundeberg et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid

molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (i.e. module-binding site), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (module) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element (via additional modules, Column 4, lines 9-11) and immobilizing the polynucleotide-targeting element-separation group complex and isolating the complex (Column 11, lines 7-14) wherein the polynucleotide of interest is genomic DNA (Column 4, lines 43-45) but they do not teach specific diagnostic application e.g. detection of single nucleotide polymorphism (SNP).

Engelhardt et al teach a similar method of separating genomic DNA of interest and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23 and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the genomic DNA analysis of Lundeberg et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

**Conclusion**

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables

applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
November 4, 2004